Research Study Information

About computer-assisted image analysis in the diagnostic workup of rare genetic disorders

Ladies and gentlemen,

you or your child is suspected of having a genetic disorder. During the workup of differential diagnoses, phenotypic features (e. g. the face) can provide important information. Computer-assisted methods of image analysis are increasingly being used to assess the external appearance. These **next-generation phenotyping (NGP)** approaches are used to identify patterns on the basis of photographs and calculate similarities to patients with already confirmed genetic disorders. NGP can assist the physician in selecting a specific molecular genetic test. NGP can also be used for interpreting the results of molecular genetic investigations.

In our research study, the quality of the currently available image analysis methods (e. g. Face2Gene) will be investigated. Furthermore, we will also investigate whether a new protocol for evaluating mutations, called PEDIA (prioritization of exome data by image analysis) will improve the diagnostic yield.

If our research study shows that NGP can help to find the right diagnosis more quickly, unnecessary examinations can be avoided in the future and patients will receive appropriate medical care earlier for their specific disease.
Our study is aimed at improving the diagnosis of genetic diseases and will also contribute to their successful treatment in the long term. However, participation in this project is unlikely to have any direct therapeutic benefit for you.

Within the routine diagnostic workup, the clinical abnormalities are documented by means of photos and medical terminology. The phenotypic characteristics, as well as photos or results of the image analysis are sent to us by your doctor in pseudonymized form. Pseudonymization means that we do not know the name or address of the study participant. The clinical data can only be assigned to a person by means of a numerical code that is available to the submitter (see also the supplemental material explaining the transmitted data).

All data from the research study will be stored on a server at the Institute of Genomic Statistics and Bioinformatics, in Bonn, Germany, which complies with current data protection regulations.

We intend to publish the results of this research project in scientific journals and at conferences. These publications will not contain any personal information that allows you to be identified.

Participation in the study is free of charge. There is no entitlement to remuneration or other financial benefits and profits that may be obtained on the basis of the research.

Participation in this investigation is completely voluntary. The informed consent may be withdrawn at any time and without giving reasons. In the event of a revocation of consent, all data attributable to your pseudonym will be deleted. You will not suffer any disadvantages.

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Supplemental Material: Explanation of data transfer using from Face2Gene

Next-generation phenotyping uses artificial intelligence to analyze photos. First of all, certain facial areas such as mouth, nose and eyes are identified on the photo and compared with pre-training phenotype models for known syndromes. A detailed description of the methodology can be found in the work "DeepGestalt-Identifying Rare Genetic Syndromes Using Deep Learning". (https://arxiv.org/pdf/1801.07637.pdf)
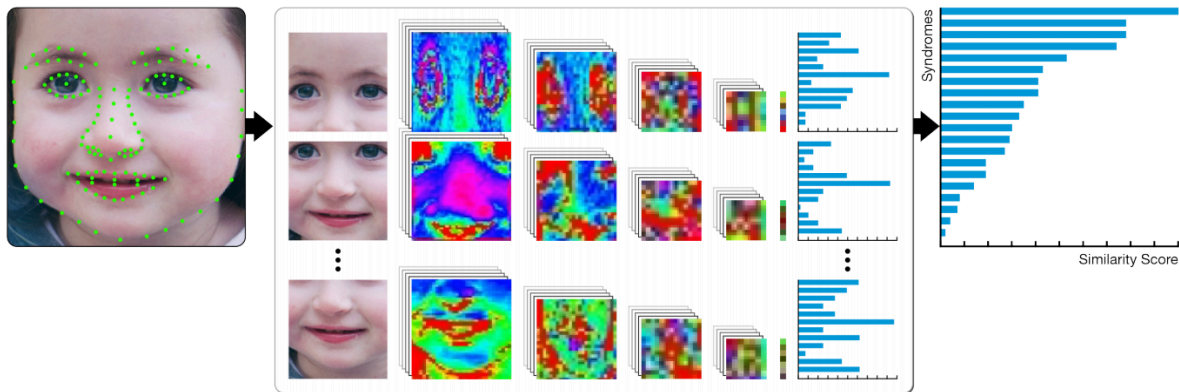
As a result of the image analysis, similarity values ("gestalt scores") to all known syndromes are calculated by the software Face2Gene.

The "gestalt scores" can be transferred to us pseudonymized via an electronic interface (Face2Gene Labs API).

Example of transmitted data:

```
{
    "case_id": 31294,         # this is the pseudonym of the study participant
    "features": [
      "HP:0100543",           # this ID encodes the phenotypic feature „cognitive impairment".
      "HP:0002345",
      "HP:0001234"
    ],

    "detected_syndromes": [
    { "omim_id": 117550,  # this ID stands for Sotos syndrome
      "feature_score": 0.42
      "gestalt_score": 0.12
    }
        .
        .
        .
    ],
    "submitter": {
      "user_email": "studydoctor@email.edu",
    }
  }
```

If you have any further questions, don't hesitate to contact us:

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